REVIEW ARTICLE

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The impact of air pollution and heavy metal exposure on the risk of coeliac disease in the paediatric population

Wpływ zanieczyszczeń powietrza i metali ciężkich na ryzyko wystąpienia choroby trzewnej (celiakii) w populacji pediatrycznej

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A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

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Abstract

Introduction and Objective. Coeliac disease is a chronic autoimmune disorder of the small intestine that develops in genetically predisposed individuals (HLA-DQ2/DQ8) following gluten exposure. Although genetic factors play a pivotal role in its pathogenesis, the rising incidence observed over recent decades suggests that environmental factors also contribute. The aim of the review is to analyze recent data regarding the influence of air pollution and heavy metal exposure on the risk and course of coeliac disease in children and adolescents.

Brief description of the state of knowledge. An increasing number of studies indicate that heavy metals and air pollutants may contribute to the development and progression of coeliac disease. Nanoparticles of silver, titanium dioxide, and gold disrupt the gut microbiota, damage the intestinal barrier, and activate the immune system, elevating pro-inflammatory cytokines such as IL-15, IFN-γ, and IL-8. Exposure to heavy metals is associated with over-representation of Bacteroides and Firmicutes, impaired tight junctions, and disrupted autophagy in enterocytes, all promoting intestinal injury. Individuals on gluten-free diets, especially those rich in rice-based products, may accumulate more heavy metals, exacerbating mucosal damage. Likewise, pollutants like nitrogen dioxide, particulate matter, and ozone weaken gut integrity, alter immune responses, and are linked to increased coeliac disease prevalence, particularly in children in polluted areas.

Summary. Heavy metals and air pollution may alter the intestinal microenvironment, epithelial barrier function, and immune response, representing potential risk factors for the development of coeliac disease. Their role in the disease's pathogenesis warrants further multicentre, multidisciplinary research.

Key words

immune response, heavy metals, environmental pollution, coeliac disease, environmental factors, children

Streszczenie

Wprowadzenie i cel pracy. Celiakia to przewlekła choroba autoimmunologiczna jelita cienkiego, rozwijająca się u osób z predyspozycją genetyczną (HLA-DQ2/DQ8) po ekspozycji na gluten. Mimo że czynniki genetyczne odgrywają kluczową rolę w jej patogenezie, obserwowany w ostatnich dekadach wzrost liczby zachorowań sugeruje wpływ także czynników środowiskowych. Celem pracy było przeanalizowanie najnowszych danych dotyczących wpływu zanieczyszczeń powietrza oraz ekspozycji na metale ciężkie na ryzyko rozwoju i przebieg choroby trzewnej u dzieci i młodzieży.

Opis stanu wiedzy. Coraz więcej badań wskazuje, że metale ciężkie mogą odgrywać rolę w powstaniu i nasileniu celiakii. Nanocząstki srebra, tlenku tytanu i złota zaburzają mikrobiom jelitowy, uszkadzają barierę śluzówkową i aktywują układ odpornościowy, zwiększając poziom cytokin prozapalnych (m.in. IL-15, IFNγ, IL-8). U chorych obserwuje się nadmiar bakterii z rodzaju *Bacteroides* i *Firmicutes*, co może być skutkiem ekspozycji na metale. Dodatkowo związki te upośledzają integralność połączeń między komórkami nabłonka i zaburzają autofagię w enterocytach, sprzyjając destrukcji jelita cienkiego. Osoby na diecie bezglutenowej są też bardziej narażone na akumulację metali (np. z ryżu), co może nasilać uszkodzenia. Zanieczyszczenia powietrza, takie jak NO_2, pyły PM i ozon, także uszkadzają barierę jelitową, wpływają na odporność i zwiększają ryzyko celiakii. Wśród dzieci choroba trzewna częściej diagnozowana jest u tych, które mieszkają w rejonach o większym zanieczyszczeniu.

Podsumowanie. Metale ciężkie i zanieczyszczenia powietrza mogą wpływać na mikrośrodowisko jelitowe, barierę nabłonkową i odpowiedź immunologiczną, stanowiąc potencjalne czynniki ryzyka rozwoju celiakii. Ich rola w patogenezie tej choroby wymaga dalszych, wieloośrodkowych badań.

Słowa kluczowe

odpowiedź immunologiczna, metale ciężkie, zanieczyszczenia powietrza, choroba trzewna, czynniki środowiskowe, dzieci

INTRODUCTION

Coeliac disease is a chronic autoimmune disorder characterized by T-cell-mediated inflammation of the

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proximal small intestine and villous atrophy in genetically predisposed individuals in response to dietary gluten exposure [1–6]. It is important to note that coeliac disease should not be regarded as a typical autoimmune disorder, as the triggering factor – gluten – is exogenous and is obtained from the diet [7].

Genetic predisposition plays the most significant role in the pathogenesis of coeliac disease, similar to other autoimmune conditions, which is evidenced by the strong association with specific human leukocyte antigen (HLA) variants, primarily HLA-DQ2 and HLA-DQ8. However, despite carrying these genetic risk factors, only about 3–5% of individuals develop the disease [2, 3].

Gluten comprises a group of storage proteins found in wheat and related cereal grains, such as barley and rye. In coeliac disease, deamidated gluten peptides are presented by antigen-presenting cells expressing HLA-DQ2 or HLA-DQ8 molecules to CD4+ T lymphocytes. This process activates gluten-specific T cells, resulting in cytokine secretion and the production of autoantibodies against tissue transglutaminase (tTG) and endomysium (EMA), ultimately leading to small intestinal mucosal damage [7].

Complete elimination of gluten from the diet remains the most effective treatment for coeliac disease [1–7].

It is estimated that approximately 1% of the global population is affected by coeliac disease, with minor geographical variations [2, 4, 6, 7]. Although diagnosis is most often made in childhood, the non-specific clinical presentation in children can frequently delay diagnosis until adulthood. Currently, intestinal biopsy is no longer required for diagnosis in children, unlike practices from several years ago [5, 6].

In recent decades, a significant increase in the incidence of coeliac disease has been observed, which cannot be fully explained by genetic factors alone [3, 4, 7]. This rise is now largely attributed to environmental factors, as well as improved awareness among gastroenterologists and more sensitive and specific diagnostic methods [3, 4, 7]. In recent years, experts have focused on the impact of environmental factors on population health [1]. Among the most critical environmental determinants contributing to the deterioration of health status and the development of numerous diseases are heavy metals and air pollutants [1–3]. Exposure to these factors has been associated with an elevated risk of cardiovascular, respiratory, neurological disorders, as well as malignancies. Given their ubiquity, chronic population-wide exposure, and the absence of a safe threshold of action, they represent a key area of ongoing research [1, 2].

Of particular importance is their role in the pathogenesis of autoimmune diseases, including celiac disease [1, 2, 4–6]. Heavy metals such as cadmium, lead, and arsen, through bioaccumulation and induction of oxidative stress, may impair immune responses and compromise the integrity of intestinal barrier, whereas air pollutants promote chronic inflammation, gut dysbiosis, and modulation of the gut–immune axis. Undoubtedly, these mechanisms play a significant role in the initiation and progression of autoimmune processes [1, 4, 6].

OBJECTIVE

The aim of this study is to review the available scientific literature regarding the potential impact of air pollution and heavy metal exposure on the risk, development, and course of coeliac disease in children and adolescents. The study seeks to evaluate whether environmental factors, alongside known genetic and dietary determinants, play a significant role in the pathogenesis of this autoimmune disorder.

MATERIALS AND METHOD

The studyis an unsystematic literature review which involved searching the databases PubMed, Google Scholar, and Scopus for the period from 1 January 2020 – 31 May 2025. The search strategy used English key words: coeliac disease, air pollution, heavy metals, environmental exposure, autoimmune diseases, paediatric, children, and environmental risk factors. Only articles published in English were considered.

The review included original research articles, review papers, and meta-analyses published within the last five years that focused on children and adolescents up to 18 years of age diagnosed with coeliac disease, and examining the impact of exposure to air pollution and/or heavy metals on the risk, development, or course of the disease. Priority was given to observational studies, such as cohort and cross-sectional studies, as well as selected clinical trials.

STATE OF KNOWLEDGE

Pathomechanism of the disease. The etiology of coeliac disease is multi-factorial, involving a complex interplay of genetic, environmental, and immunological factors [8]. Gluten, upon ingestion, is broken down in the gastrointestinal tract by digestive enzymes into gliadin peptides containing glutamine residues. Tissue transglutaminase catalyzes the deamidation of glutamine to glutamic acid, resulting in the formation of deamidated gliadin peptides (DGP), which are highly immunogenic and exhibit increased affinity for specific human leukocyte antigen (HLA) molecules [2, 6, 7].

Genetic predisposition is observed in individuals expressing HLA-DQ2 and/or HLA-DQ8 molecules. The susceptibility to coeliac disease strongly depends on the presence of these genotypes [8, 9]. These genes encode MHC class II molecules expressed on antigen-presenting cells (APCs), which present deamidated gliadin peptides to CD4+ T helper cells. This interaction promotes the activation and differentiation of intraepithelial lymphocytes (IELs) into cytokine-activated cytotoxic effector cells [6, 8, 9], which mediate epithelial cell apoptosis primarily through mechanisms independent of classical T cell receptors [9, 10].

Pro-inflammatory cytokines, particularly interleukin-15 (IL-15), further enhance the cytotoxic potential of IELs, contributing to chronic inflammation, epithelial damage, and the development of villous atrophy, hallmarks of coeliac disease [10]. HLA-DQ2 expression is present in over 90% of individuals with coeliac disease. A negative result for both HLA-DQ2 and HLA-DQ8 virtually excludes the diagnosis of this condition [11].

Recent studies have identified an elevated presence of novel T cell subsets, including CD4+CD25+ regulatory T

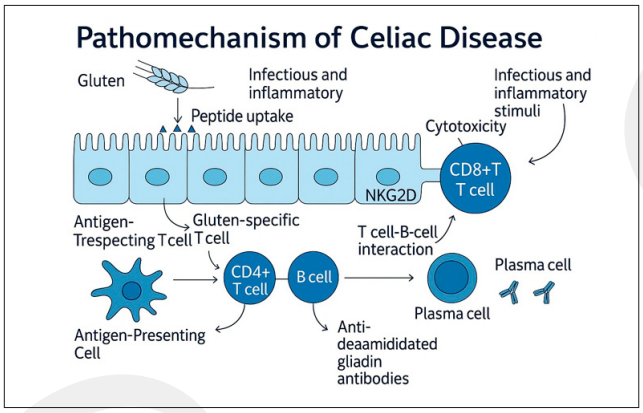

Figure 1. Pathomechanism of coeliac disease

cells (Tregs) and Th17 cells, during active disease phases, implicating them in the disease's inflammatory response [11]. Additionally, B lymphocytes are involved in the immunopathogenesis of coeliac disease. Upon activation through HLA-mediated interactions, they differentiate into plasma cells that produce disease-specific autoantibodies targeting tissue transglutaminase (tTG), endomysium (EMA), and deamidated gliadin peptides (DGP) [6,9,10]. Although the exact functional role of these antibodies is not fully understood, studies have shown that they may deposit within the sub-epithelial layer of the small intestinal mucosa, even in the absence of histological abnormalities or detectable circulating autoantibodies, and without overt epithelial injury [11].

The intestinal microbiota has also been recognized as a contributing factor in the pathogenesis of coeliac disease [6, 8, 12]. A balanced gut microbiome plays a pivotal role in the physiological maturation of the gut immune system, promoting immune tolerance through the regulation of immunoglobulin and cytokine expression [13]. Alterations in the composition of gut microbiota have been documented in patients with coeliac disease, both during active disease and while adhering to a gluten-free diet [11, 12]. Emerging evidence suggests that gut bacteria may influence the activation of CD4+ T cells and contribute to the breakdown of oral tolerance to gluten in genetically-susceptible individuals [12]. Notably, dysbiosis may precede the clinical onset of disease, supporting its potential role in the initiation of autoimmune responses to gluten [12,13]. It may also explain the variability in patient sensitivity to different gluten sources, possibly due to differences in bacterial populations and the proteolytic enzymes they produce [12].

Furthermore, environmental factors such as intestinal infections, antibiotic-induced disruption of the microbiota, and exposure to environmental pollutants and heavy metals are increasingly investigated for their roles in the pathomechanism of coeliac disease [9, 11].

Diagnosis. The diagnosis of coeliac disease is a complex process that requires the integration of clinical symptoms, laboratory indicators of malabsorption, the presence of disease-specific antibodies in serum, and characteristic histopathological findings [1].

Serological markers. Currently, serological testing is considered the gold standard in the diagnostic workup of coeliac disease [6]. IgA-class antibodies against tissue transglutaminase type 2 (tTG2), the primary autoantigen in coeliac disease, represent a highly sensitive and specific marker (sensitivity and specificity above 95%) for the active form of the disease in individuals consuming gluten. Measurement of these antibodies, often preceded by determination of the total serum IgA levels – to rule out selective IgA deficiency – is regarded as the most effective first-line screening test for coeliac disease [6, 14–16].

Testing for IgG anti-tTG2 antibodies, although diagnostically less accurate than IgA-based assays, is recommended for individuals with selective IgA deficiency. These antibodies can be detected using various techniques, including ELISA, indirect immunofluorescence, radioimmunoassay, and chemiluminescence assays. However, inter-assay variability may occasionally lead to diagnostic uncertainty [6, 17].

Anti-endomysial antibodies (EMA), of the IgA class and directed against TG2 localized in the endomysium, are detected via indirect immunofluorescence using monkey oesophagus or human umbilical cord tissue substrates. EMA testing demonstrates near 100% specificity, exceeding even that of IgA anti-tTG2 assays [6, 7].

Genotyping for HLA-DQ2 and HLA-DQ8 can assist in ruling out coeliac disease, as the risk is extremely low in the absence of both alleles. HLA testing is also useful in individuals already on a gluten-free diet when the diagnosis remains uncertain [6].

Small intestinal biopsy. At present, histopathological confirmation is not mandatory for the diagnosis of coeliac disease in paediatric patients. Due to advances in serological testing, duodenal biopsy is performed to confirm the diagnosis in approximately 50% of cases [7, 15, 18].

Typical histological findings in coeliac disease include villous atrophy, crypt hyperplasia, and an increased number of intraepithelial lymphocytes (IELs). However, these changes may vary significantly from isolated duodenal lymphocytosis to complete villous flattening, and are not pathognomonic for coeliac disease, especially in cases of milder mucosal injury [6, 19].

During upper gastrointestinal endoscopy usually performed under general anesthesia it is recommended to obtain biopsy samples from both the duodenal bulb (D1) and the second (D2) and third (D3) parts of the duodenum. Limiting biopsies to the bulb alone may result in false-negative findings [7, 18].

Histopathological assessment of the small intestine is commonly based on various classification systems, with the modified Marsh-Oberhuber classification being the most frequently used [6, 7].

Clinical manifestations. The clinical presentation of coeliac disease is highly heterogeneous, which is why the medical literature distinguishes three primary forms of the disease: classical, non-classical, and sub-clinical [1, 6, 11]. Classical symptoms include chronic diarrhea, steatorrhea, abdominal pain, bloating, and weight loss, primarily resulting from maldigestion and malabsorption associated with villous atrophy of the small intestine [6, 11].

However, the non-classical form is currently the most frequently observed, characterized by non-specific gastrointestinal complaints such as recurrent abdominal pain, digestive discomfort, bloating, and constipation. These

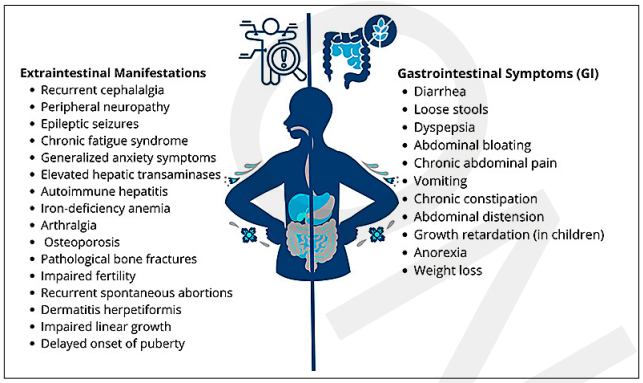

Figure 2. Gastrointestinal symptoms and extraintestinal manifestations of coeliac disease

symptoms may delay the diagnostic process and are often misinterpreted as functional gastrointestinal disorders or irritable bowel syndrome (IBS) [1, 6, 21]. As a result, there is often a significant delay between the onset of symptoms and a definitive diagnosis, which, according to recent studies, can span up to 10 years [1].

Systemic manifestations such as chronic fatigue, unintended weight loss, anaemia, or generalized urticaria, may also occur in affected individuals. Gastrointestinal and extraintestinal symptoms associated with celiac disease are illustrated in Figure 2.

The classical form is most commonly diagnosed in children under the age of five [6]. Subclinical coeliac disease is typically identified through laboratory abnormalities and imaging findings, often as part of population-based screening programmes or targeted testing in high-risk groups, such as first-degree relatives of coeliac patients [6, 11].

In untreated patients or those with an inadequate clinical response to therapy, deficiencies in electrolytes, vitamins, and minerals may develop [6, 20, 21]. Refractory coeliac disease (RCD) is defined as persistent activation of the immune system, villous atrophy, and malabsorptive symptoms, despite strict adherence to a gluten-free diet for at least one year [21]. Recent studies indicate that up to 90% of patients with active coeliac disease may exhibit nutritional deficiencies with clinically significant consequences [21]. The most common deficiency is iron deficiency – anaemia, present in approximately 50% of patients at diagnosis. In some cases, anaemia may be the only presenting sign suggestive of subclinical coeliac disease [6, 22]. Additional deficits may involve folic acid, vitamin B12, vitamin D, and zinc metabolism [11, 21].

Among the complications of untreated coeliac disease, neurological manifestations are prominent and include chronic headaches, 'gluten-induced neuropathy', likely mediated through molecular mimicry between gluten and ganglioside antigens of peripheral nerves gluten ataxia, and a higher incidence of epilepsy [1, 6, 21]. Dermatological complications such as eczema, psoriasis, urticaria, and dermatitis herpetiformis are also reported. Patients may experience increased musculoskeletal pain, osteopenia and osteoporosis, dental enamel defects, and short stature, particularly in the paediatric population [1, 6, 21]. It is also important to note that coeliac disease, as an autoimmune disorder, often coexists with other autoimmune conditions, such as type 1 diabetes mellitus, Hashimoto's thyroiditis, or Sjögren's syndrome [6, 20].

Treatment. Currently, the cornerstone of coeliac disease management is the lifelong adherence to a strict gluten-free diet, aimed at complete elimination of dietary gluten [1, 7]. Despite extensive research efforts, no pharmacological therapy has yet been developed that addresses the underlying cause of coeliac disease, such as restoring immunological tolerance to gluten or halting the immune response at any stage of the inflammatory cascade [1].

Children diagnosed with coeliac disease must strictly avoid all gluten-containing grains, including wheat, rye, barley, and their derivatives. Products made from these cereals, such as bread and pasta, are strictly prohibited. Conversely, naturally gluten-free grains and pseudo-cereals, including rice, corn, buckwheat, amaranth, quinoa and millet, are permitted, provided they have not been contaminated with gluten during processing [23, 24].

According to international regulatory guidelines, a product labelled as 'gluten-free' must contain no more than 20 mg of gluten per kilogram to be considered safe for individuals on a gluten-free diet [23]. It is important to recognize that children on a gluten-free diet are at increased risk of macro- and micronutrient deficiencies, particularly in calcium, iron, dietary fiber, and various vitamins and minerals [6, 7, 25, 26]. Moreover, commercially available gluten-free products often contain higher levels of simple sugars and fats compared to their gluten-containing counterparts. Nevertheless, current evidence does not support an increased prevalence of obesity or hypercholesterolemia among children following a gluten-free diet [27].

While the ingestion of trace amounts of gluten may not produce overt clinical symptoms, it can still impair intestinal mucosal integrity, elevate the risk of pathological fractures, and contribute to the development of lymphoproliferative malignancies. However, such low-level exposure does not appear to affect overall life expectancy [1, 6].

Adjunctive treatments with probiotic supplementation have also been explored [6]. A 2020 meta-analysis suggested that probiotics may alleviate persistent gastrointestinal symptoms in some coeliac patients adhering to a gluten-free diet, although the quality of available evidence remains low [28].

In cases of refractory coeliac disease (RCD), where mucosal damage and malabsorptive symptoms persist despite strict dietary adherence for at least 12 months, more advanced therapeutic approaches are necessary. These include nutritional support and immunosuppressive therapy. First-line pharmacological options consist of oral budesonide combined with azathioprine, while second-line regimens may include oral budesonide or intravenous prednisone, cladribine, and, in type 2 RCD cases unresponsive to standard treatment, autologous hematopoietic stem cell transplantation [29, 30].

IMPACT OF ENVIRONMENTAL FACTORS ON THE RISK AND COURSE OF COELIAC DISEASE

Heavy metals. Exposure to environmental pollution, including heavy metals, is currently recognized as a significant risk factor for numerous diseases and deterioration in health outcomes across the general population [31, 32]. Recent epidemiological studies suggest a correlation between heavy metal contamination in the environment and disruptions in

the host's microbiological and immunological homeostasis [31]. Heavy metal exposure impairs the metabolic activity of the gut microbiome, inducing inflammatory responses and cellular damage. Conversely, restoration of microbiome balance and sequestration of heavy metals by specific microbial populations may confer potential benefits to the host [31, 32].

Numerous ongoing studies are investigating the direct effects of heavy metals on the incidence of coeliac disease, as the precise mechanisms and long-term impact of these toxins on its etiology remain incompletely understood [31, 32]. Alterations in the gut microbiome and intestinal barrier integrity induced by heavy metal nanoparticles may potentially contribute to various inflammatory diseases, including coeliac disease, which is also associated with reduced microbial diversity and richness compared to healthy controls [31, 32].

One study demonstrated that silver (Ag) and titanium dioxide (TiO_2) nanoparticles increased the abundance of Bacteroides species, which are found in significantly higher numbers in stool samples and intestinal biopsies of patients with coeliac disease compared to the general population [32]. Additionally, TiO_2 nanoparticles elevated levels of Firmicutes, which are more prevalent in infants genetically predisposed to coeliac disease [32]. Notably, levels of Faecalibacterium prausnitzii were lower in these patients compared to healthy individuals, a change potentially linked to silver nanoparticle exposure [32]. These findings suggest that heavy metal nanoparticles may modulate gut microbiota in patterns mimicking those observed in coeliac disease [32].

Further research examined the combined effects of digested gliadin the main immunogenic component of gluten with silver and gold nanoparticles on a human intestinal crypt-like epithelial cell line. The study aimed to demonstrate that heavy metal nanoparticles can interact with gliadin and trigger an immune response. This combination was shown to block autophagic flux by inducing lysosomal dysfunction. Disruption of this pathway, essential for cellular homeostasis, may lead to epithelial cell damage and death, potentially initiating pathogenic processes within the intestinal mucosa of coeliac patients [33]. Moreover, heavy metal nanoparticles were shown to alter the thickness and composition of the mucus layer, with observed reductions in villus-to-crypt ratios and histological features resembling coeliac disease [33, 34].

A Chemical–Gene Set Enrichment Analysis (CGSEA) conducted in 2022 in the context of coeliac disease confirmed that heavy metals, particularly cadmium and arsenic, disrupt the tight junctions between intestinal epithelial cells [35]. Compromised intestinal barrier function increases permeability, facilitating the translocation of antigens and toxins into the submucosa and triggering immune activation. This phenomenon may exacerbate the autoimmune response typical of coeliac disease, even in the absence of gluten as a triggering factor [34, 35].

Additionally, heavy metals can generate reactive oxygen species (ROS), leading to oxidative stress in intestinal cells. This is linked to activation of dendritic cells, Th1 lymphocytes, and pro-inflammatory cytokines that play a key role in coeliac disease pathogenesis. Up-regulation of inflammation-related genes may perpetuate chronic intestinal mucosal inflammation. For instance, gold nanoparticles induced IFN-γ expression, silver treatment increased IL-15 and IFN-γ levels, while titanium dioxide elevated IL-8, TLR2, and IFN-γ all inflammatory mediators involved in coeliac disease pathophysiology [34, 35].

An additional intriguing issue is the relationship between heavy metals and the gluten-free diet. Population studies have identified fish and rice products as potential sources of heavy metals, and individuals adhering to a gluten-free diet exhibited significantly higher levels of metals in blood and urine compared to controls [35, 36].

It has been suggested that coeliac patients, especially children and pregnant women, may be particularly susceptible to the toxic effects of heavy metals from gluten-free products. Nevertheless, a gluten-free diet remains unequivocally the most effective treatment for coeliac disease, emphasizing the need for further research to clarify the long-term consequences of heavy metal accumulation associated with this dietary approach [33, 35, 36].

Air pollution. Environmental factors, including air pollution, appear to be a significant risk factor for the development of coeliac disease, second only to genetic predispositions. This is supported by the fact that only a small percentage of individuals positive for HLA-DQ2 or HLA-DQ8, who consume gluten-containing foods, actually develop coeliac disease [4, 6, 7, 37].

Currently, there is limited research in the medical literature investigating the impact of environmental pollution on the risk of coeliac disease development. However, all existing studies highlight a significant association between airborne particulate matter and increased incidence of coeliac disease in children [38, 39]. Data indicate that exposure to air pollutants such as nitrogen dioxide, particulate matter, and ozone may elevate the risk of coeliac disease [40]. These pollutants disrupt the integrity of the intestinal epithelium and modulate the local immune response, potentially leading to impaired immunological tolerance to gluten and initiating the chronic inflammatory process characteristic of coeliac disease [40].

Changes in the gut microbiota observed in infants at high risk for coeliac disease due to environmental factors further underscore the critical role of the environment in the disease's pathogenesis [41]. Moreover, short-term increases in air pollution concentrations have been linked to exacerbation of gastrointestinal inflammatory symptoms and increased hospitalizations for autoimmune diseases, suggesting a dose-response relationship and emphasizing the importance of monitoring environmental exposure [40, 42].

In a pilot study, Gaylord A. et al. investigated whether persistent organic pollutants present in the air might serve as potential risk factors for coeliac disease development. Despite a small sample size, an increased likelihood of the disease was observed in association with certain POPs, particularly dichlorodiphenyldichloroethylene, although these estimates were imprecise. The authors suggested that these compounds may influence the severity of intestinal inflammation and play a role in differentiating symptomatic and asymptomatic forms of coeliac disease. Gender differences were also noted: stronger associations in women were found with compounds from the per- and polyfluoroalkyl substances group, whereas in men the association was observed only with polybrominated diphenyl ether (BDE-153) [38].

In light of these findings, further research integrating epidemiological data, immunological studies, and multi-omics analyses is necessary to better elucidate the mechanisms

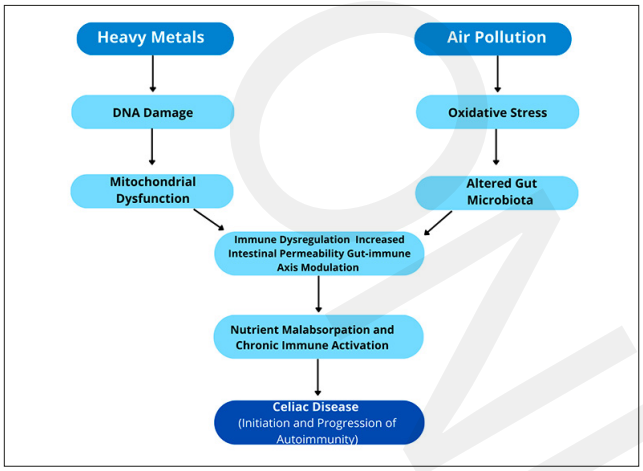

Figure 3. Heavy metals and air pollution vs coeliac disease

by which air pollution influences the development and course of coeliac disease.

The associations between exposure to heavy metals and air pollution and the risk of coeliac disease are presented in Figure 3.

Limitations of the review. This study is a non-systematic review of the literature, which entails certain methodological limitations. First, the lack of a fully systematic search strategy increased the risk of selective inclusion of sources and limits the representativeness of the analyzed studies. Second, only publications in English were included, which may have led to the omission of relevant studies published in other languages. Third, the analysis was restricted to articles published between 2020–2025, which precluded consideration of earlier research findings. Another limitation concerns the age criterion – only studies involving children and adolescents up to 18 years of age were included, which prevented extrapolation of the conclusions to adult populations. Furthermore, only full-text publications were analyzed, while descriptive reports, single case studies, letters to the editor, and commentaries were excluded, which may have narrowed the scope of perspectives considered. In addition, studies focusing exclusively on genetic or dietary factors were also excluded, meaning that the conclusions do not cover the full spectrum of potential determinants of the onset and course of celiac disease.

Given these limitations, the conclusions presented should be interpreted with caution and regarded as a contribution to further, more systematic analyses.

SUMMARY

In light of the available data, it can be concluded that heavy metals and other environmental pollutants constitute a significant, yet still insufficiently understood, component in the etiopathogenesis of coeliac disease. Their impact on the gut microbiome, as well as their direct effects on intestinal epithelial cells, may represent additional risk factors which, in genetically predisposed individuals, promote the development and progression of the disease. Therefore, further research on the role of heavy metals in the pathogenesis of coeliac disease is essential to better understand the environmental mechanisms underlying this condition and to develop effective preventive and therapeutic strategies.

Exposure to heavy metals and air pollution affects the gut microbiota, epithelial barrier integrity, and immune response, which may contribute to the development and progression of celiac disease. Available studies simultaneously highlight the necessity of further interdisciplinary research to fully elucidate the mechanisms underlying these environmental factors and their long-term health consequences.

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